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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/535,043

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EXAMINER

ZAREK, PAUL E

ART UNIT

PAPER NUMBER

1617

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02/06/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/535,043	Applicant(s) DOWNES ET AL.	
	Examiner Paul Zarek	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/10/2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14, 21 and 24-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14, 21, and 24-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/10/2008</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

1. Claims 1-3 have been amended and Claims 36 and 37 have been cancelled by the Applicant in correspondence filed on 12/10/2008. Claims 1-14, 21, and 24-26 are currently pending. This is the second Office Action on the merits of the claim(s).

RESPONSE TO ARGUMENTS

2. Claims 1, 4-14, 21, and 24-26 were rejected under 35 U.S.C. 112, first paragraph, as not being fully enabled for a method of modulating process(es) mediated by farnesoid X receptor polypeptides. This rejection is moot in light of Applicants' amendments to Claim 1, from which 4-14, 21, and 24-26 depend.

3. Claims 1-14, 21, and 24-26 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is moot in light of Applicants' amendments to Claim 1-3, from which 4-14, 21, and 24-26 depend.

4. Claim 12 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite due to a lack of antecedent basis for R^3 as $-\text{CH}=\text{CH}-\text{C}(\text{O})-\text{O}-\text{tBu}$. This was based on the fact that Claim 12 depends upon Claim 11, in which R^3 was limited to alkenyl. The instant specification defines alkenyl as a "straight or branched chain hydrocarbonyl group having at least one carbon-carbon doublebond, and having in the range of about 2 up to 20 carbon atoms" (paragraph 0010). Applicants state that alkenyl embraces ethenyl and that the tert-butoxycarbonyl substitution is

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encompassed by “alkenyl.” Examiner respectfully disagrees. The presence of the –O– is not encompassed by the definition of "alkenyl" in the specification. It is encompassed by “substituted alkenyl.” Therefore, the rejection of Claim 12 under 35 U.S.C. 112, second paragraph, is maintained. Amending the claim to read "substituted alkenyl" would overcome this rejection.

5. Claims 1-14, 21, 24-26, 36, and 37 were rejected on the grounds of nonstatutory obvious-type double patenting over copending application 10/535,041. As discussed in the interview, and reiterated in Applicants’ response, this rejection was inappropriately applied. Therefore, the rejection is withdrawn.

6. Applicants submitted an IDS with a fee according to the time period set forth in MPEP § 609.04(b)(II). Therefore, the following **FINAL** rejection is made.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1-14, 21, and 24-26 are rejected under 35 U.S.C. 102(e) as being anticipated by Nicolaou, et al. (International Application No. WO 04/046162, provided in IDS). Examiner notes that Nicolaou, et al, claims priority to US Provisional Application 60/426,456, filed on

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11/14/2002. The instant application claims the benefit of US Provisional 60/426,664, filed on 11/15/2002. It is noted that Nicolau, Roecker, and Hughes are listed inventors on both provisional applications.

9. Claim 1 of the instant application is drawn to a method of treating hypercholesteremia or cholestasis comprising administration of the formula disclosed in Claim 1. Claims 2 and 3 limit the method to treat hypercholesteremia and cholestasis, respectively. Claims 4-14, 21, and 24-26 further limit the various subgroups of the formula of Claim 1.

10. Nicolaou, et al., disclose all of the compounds encompassed by the claims of the instant application. It is noted Figures 20(a-d), and 28 disclose compounds and the corresponding EC₅₀ values for the farnesoid X receptor that are identical to those compounds and EC₅₀ values described in Tables 1-15 of the instant application. Nicolaou, et al., explicitly state that the "FXR agonists of the present invention can be employed as therapeutic agents for the treatment of diseases linked to cholesterol, bile acids, and their metabolism and homeostasis" (pg 5, lines 2-4). Support for the treatment of cholestasis and hypercholesteremia is in the provisional application from which Nicolaou, et al., claim benefit. "FXR modulators may find potential utility in the treatment of cholestasis and other disease states associated with aberrant levels, flow, and release of bile acids" (pg 1, lines 24-26).

11. In correspondence filed on 12/10/2008, Applicants allege that Nicolaou, et al., do not provide enabling support for the treatment of cholestasis and hypercholesteremia. Applicants are correct that Nicolaou, et al., if read in a vacuum, would not enable a skilled artisan to treat cholestasis and/or hypercholesteremia. However, if the instant application were read in a similar vein (e.g. without knowledge of the state of the art), it would not be enabling for the treatment of

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cholestasis and/or hypercholestermia. Indeed, akin to Nicolaou, et al., the instant application provides only generic contemplation of treating these disorders. "These compounds are useful as chemical tools to further define the physiological role of FXR as well as therapeutic leads for the treatment of diseases linked to cholesterol, bile acids and their metabolism and homeostasis" (pg 3, lines 5-7).

12. The instant application was deemed enabled for the treatment of cholestasis and hypercholestermia because the state of the art at the time of the invention demonstrated that FXR agonists can inhibit cholesterol metabolism. Applicants' demonstration that the claimed compounds were effective agonists for the FXR was sufficient for enabling support. By the same token, the state of the art provided enabling support for the generic teaching of utilizing the compounds taught by Nicolaou, et al., for the treatment of cholestasis and hypercholestermia. Put another way, art that enables the instant application also enabled Nicolaou, et al. Therefore, Nicolaou, et al., anticipate all the limitations of the rejected claims.

Conclusion

13. Claims 1-14, 21 and 24-26 are rejected

14. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 12/10/2008 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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PEZ

/Rita J. Desai/
Primary Examiner, Art Unit 1625